

Identification of Candidate miRNA Biomarkers for Glaucoma

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PURPOSE: Glaucoma, a leading cause of blindness worldwide, often remains undetected until irreversible vision loss has occurred. Treatments focus on lowering intraocular pressure (IOP), the only modifiable and readily measurable risk factor. However, IOP can vary and does not always predict disease progression. MicroRNAs (miRNAs) are promising biomarkers. They are abundant and stable in biological fluids, including plasma and aqueous humor (AqH). We aimed to identify differentially expressed miRNAs in AqH and plasma from glaucoma, exfoliation syndrome (XFS), and control subjects.

METHODS: Plasma and AqH from two ethnic cohorts were harvested from glaucoma or XFS (often associated with glaucoma, n = 33) and control (n = 31) patients undergoing elective surgery. A custom miRNA array measured 372 miRNAs. Molecular target prediction and pathway analysis were performed with Ingenuity Pathway Analysis (IPA) and DIANA bioinformatical tools.

RESULTS: Levels of miRNAs in plasma, a readily accessible biomarker source, correlated with miRNA levels in AqH. Twenty circulating miRNAs were at least 1.5-fold higher in glaucoma or XFS patients than in controls across two ethnic cohorts: miR-4667-5p (P = 4.1×10^{-5}), miR-99b-3p (P = 4.8×10^{-5}), miR-637 (P = 5.1×10^{-5}), miR-4490 (P = 5.7×10^{-5}), miR-1253 (P = 6.0×10^{-5}), miR-3190-3p (P = 3.1×10^{-4}), miR-3173-3p (P = 0.001), miR-608 (P = 0.001), miR-4725-3p (P = 0.002), miR-4448 (P = 0.002), and miR-323b-5p (P = 0.002), miR-4538 (P = 0.003), miR-3913-3p (P = 0.003), miR-3159 (P = 0.003), miR-4663 (P = 0.003), miR-4767 (P = 0.003), miR-4724-5p (P = 0.003), miR-1306-5p (P = 0.003), miR-181b-3p (P = 0.004), and miR-433-3p (P = 0.004). miR-637, miR-1306-5p, and miR-3159, in combination, allowed discrimination between glaucoma patients and control subjects (AUC = 0.91 ± 0.008 , sensitivity 85.0%, specificity 87.5%).

CONCLUSIONS: These results identify specific miRNAs as potential biomarkers and provide insight into the molecular processes underlying glaucoma.

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